EMBRYOTOXIC AND TERATOGENIC ACTION OF PROGUANIL, CHLORPROGUANIL, AND CYCLOGUANIL ON ALBINO RATS

N. A. Chebotar'

UDC 615.283.926.015.45:612.64

The antimalarial drugs chlorproguanil, proguanil, or cycloguanil were given internally in a sublethal dose of 30 mg/kg at intervals of 4 h to rats at various periods of pregnancy. Chlorproguanil and proguanil had neither an embryotoxic nor a teratogenic action. Cycloguanil inhibited the development of the ova during cleavage. The results indicate that the teratogenic and embryotoxic effects depend on the chemical structure of the antimalarials.

Considering the possible teratogenic action of any chemical substance [2] it is advisable to study the effects of antimalarial compounds so widely given for long periods during pregnancy. Proguanil has been shown not to have any harmful action on embryogenesis in rats when given as a single dose [1]. However, this might be connected with its rapid elimination from the body.

The effect of repeated administration of chlorproguanil, proguanil, and cycloguanil on the development of rat embryos was studied.

EXPERIMENTAL METHOD

Tests were carried out on 260 pregnant albino rats weighing 180-200 g. The compounds were given by gastric tube in doses of 25 to 50 mg/kg, twice or three times at intervals of 4 h, on the 1st and the 7th-13th days of pregnancy. The results were read on the 20th day. The state of the internal organs was studied in 1170 fetuses fixed in Bouin's fluid. Control animals received water by the same route.

EXPERIMENTAL RESULTS

Chlorproguanil and proguanil, in a sublethal dose for female rats of 30 mg/kg, had neither embryotoxic nor teratogenic action. Malformations of the internal organs were found equally often in the experimental and control fetuses. Cycloguanil, when given on the 9th and 13th days of pregnancy, likewise had no harmful effect, but if it was given on the 1st day of pregnancy 90% of the embryos died. Consequently, chlorproguanil and proguanil, compounds with a linear structure, have no harmful action on the embryonic development of rats, whereas rearrangement of the proguanil molecule into the cyclic derivative, cycloguanil, gives the compound a toxic action at the stage of cleavage of the ovum.

LITERATURE CITED

1. A. P. Dyban, L. D. Udalova, and I. M. Akimova, Dokl. Akad. Nauk SSSR, 167, No. 1, 228 (1966).
2. H. Nishimura and S. Miyamoto, Acta Anat. (Basel), 74, 121 (1969).

Department of Embryology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 77, No. 6, pp. 56-57, June, 1974. Original article submitted August 13, 1973.